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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/780,752	02/09/2001	Kirk P. Conrad	CONN-001	6620

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EXAMINER
LIU, SAMUEL W

ART UNIT	PAPER NUMBER
1653	17

DATE MAILED: 05/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/780,752	CONRAD ET AL.	
	Examiner	Art Unit	
	Samuel W Liu	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15 and 28-32* is/are pending in the application.

4a) Of the above claim(s) *20-27* is/are withdrawn from consideration.

5)☒ Claim(s) *1-4, 6,12-14,28,29 and 31* is/are allowed.

6)☒ Claim(s) *5,7-11,15,30 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The response filed February 27, 2003 (Paper No. 8) as to cancellation of claims 16-19, amendment of claims 4-5 and 7-15, and addition of new claims 28-32 have been entered. Thus, pending claims 1-15 and 28-32 are under examination to the extent that they are drawn to the elected invention.

Note that the grounds of objection and/or rejection not explicitly stated and/or set forth below are withdrawn.

Declaration under 37 C.F.R. 1.132

The declaration under 37 C.F.R. 1.132 filed 27 March 2003 (Paper No. 9) is sufficient to overcome the rejection of claims 9-15 based upon Danielson et al. reference published on February 1999.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 5, 7, 8, 11, 15, 30 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 5, 7, 8, 11, 15, 30 and 32 recite "a therapeutic effect"; the recitation is unclear because nowhere in the specification has defined the recited effect, and because it is not apparent as to what consequence of administering relaxin to the subject is to be achieved; does

administering relaxin result in partial therapeutic outcome or a unfinished cure of a disorder from which the subject is suffering?

Claim Rejections - 35 USC §102

This a new ground rejection

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claim 9 is rejected under 35 U.S.C. 102(b) as being anticipated by Danielson L. A. et al. (September 1998) *J. Am. Society of Nephrology* Vol. 9, page 336A, Abstract No. A1707).

Danielson et al. teach a process of administering relaxin hormone (*e.g.*, recombinant human relaxin) via infusion method to a mammal for increasing renal vasodilation in the said mammal. The Danielson's teaching meets the limitation set forth in claim 9.

Claims 9 and 10 are rejected under 35 U.S.C. 102(a) as being anticipated by Bigazzi, M. et al. (US Pat No. 5952296).

Bigazzi et al. teach that relaxin is active on the vascular system, *e.g.*, increasing vasodilation of arterioles (see column 2, lines 52-54, and, column 8, lines 40-42), and teach that administering the relaxin to a patient (see claim 2) *via* injection causes a striking increase in the blood flow, *i.e.*, increase vasodilation, as compared with basal flow evaluated before injection

(see column 5, lines 54-64). Thus, Bigazzi et al. teachings are applied to claim 9 of the instant application.

Also, Bigazzi et al. teaches that administration dose of relaxin [human relaxin or recombinant human relaxin (see column 1, lines 33-34, Hudson et al. reference – the reference incorporated by the Bigazzi Patent)] to a mammal is 10 μg which is equivalent to about 400 μg/kg (based on that rat weight is 250 grams) (see column 7, lines 18-19). The Bigazzi et al. teaching anticipates claim 10 of the instant application.

Response to the rejection under 35 USC 102

The rejection under 35 USC 102(a) over Danielson et al. reference is withdrawn because the declaration under 37 C.F.R. 1.132 filed 27 March 2003 (Paper No. 9) overcomes the reference teaching (see also the corresponding statement *supra*).

Claim Rejections - 35 USC §103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 9-11 are rejected under 35 U.S.C. 103(a) as being obvious over Bigazzi, M. (US Pat. No. 5952296) taken with Unemori, E. (US Pat. No. 6211147).

Bigazzi et al. teach that relaxin actively acts on the vascular system to increase vasodilation of arterioles (see column 2, lines 52-54, and, column 8, lines 40-42), and teach that administering the relaxin to a patient (see claim 2) *via* injection causes a striking increase in the blood flow, *i.e.*, increase vasodilation, as compared with basal flow evaluated before injection (see column 5, lines 54-64), as applied to claim 9 of the instant application.

Additionally, Bigazzi et al. teaches that administration dose of relaxin (human relaxin or recombinant human relaxin) to a mammal is 10 μg which is equivalent to about 400 μg/kg (based on that rat weight is 250 grams) (see column 7, lines 18-19), and teach an injectable formulation (see column 6, lines 12-14). The above Bigazzi et al. teachings are applied to claims 10 and 11 of the instant application.

Bigazzi et al. do not expressly teach continuing administration (i.e., time-course administration) in order to obtain a therapeutic effect in a patient.

Unemori teaches that (i) the dosage for administering relaxin is from about 0.1 to 500 μg/kg of body weight (see column 4, lines 23-24); (ii) the relaxin is a *recombinant* human relaxin (see column 2, lines 50-51); (iii) therapeutic formulation is an injectable formulation (see column 2, lines 1-5, where recites that "formulations of human relaxin are described in Application No. 08/050,745"; now it is US Pat No. 5451572); and (iv) continuing administration is performed

over a period sufficient to obtain a therapeutic effect on the patient (see claim 1), as applied to claims 9 and 10 of the current application.

One of ordinary skill in the art would have combined the teachings of Bigazzi *et al.* and Unemori *et al.* to develop a method of increasing vasodilation in a patient comprising administering to a patient the therapeutically formulated relaxin or recombinant relaxin, because Bigazzi et al. teach a method of vasodilation enhancement and Unemori et al. especially teaches in detailed as to how to administer relaxin to the patient including a time-course administration (i.e., continuing administering route). Thus, the skilled artesian would have been motivated to incorporate the Unemori teaching with respect to the time, dosage, and route of administration into the Bigazzi's method of relaxin-directed increasing vasodilation to successfully arrive at the current invention set forth in claims 9-11.

Thus, the claimed invention was *prima facie* obvious to make and use at the time it was made.

Response to the rejection under 35 USC 103(a)

The response asserts that Bigazzi does not anticipate the instant invention as claimed, and that a disclosure of dosage for relaxin, recombinant relaxin, injectable formation, and continuing administration dose not render the instant claims (including claims 91-11) obvious (see page 13, the sixth paragraph). The applicants' argument is unpersuasive because both Bigazzi et al. do teach the subject matter of claim 9, i.e, a method of increasing vasodilation in a patient (see the rejections stated *supra*), and because the Unemori teaching is obvious over the instant claims 9-11 limitations with respect to dosage for relaxin, recombinant relaxin, injectable formation and

continuing administration. As stated in the foregoing rejection under 35 USC 103(a), the Bigazzi and Unemori patents constitute an obviousness 103 art over the claimed invention.

Claim Rejection –Obviousness Type Double Patenting

The obviousness type double patenting rejection of previous Office action (Paper No. 7) over claims 16-19 of the instant application is withdrawn in view of the canceled claims.

Prior Art

The prior art made of record and not currently relied upon in any rejections is considered pertinent to Applicants' disclosure:

- Ahokas, R. A. et al. (*Am. J. Obstet. Gynecol.* (1989) 161, 618-262) teach lack of evidence of a vasodepressor, i.e, lowering hypertension, role for relaxin in a pregnant rat based on overiectomy which removes the source of production of ovary relaxin peptide hormone. The Ahokas teaching appears to be contradictory to the subject matter of the current invention, i.e., use of relaxin in treating hypertension disorder.

  In light of Bigazzi patent which suggests that relaxin can be used as a therapeutic agent in method for treating hypertension (see abstract, and column 8, lines 50-58), it appears that a unpredictability exists between Bigazzi and Ahokas' teaching stated above. Because of this unpredictability concern, the Bigazzi et al. Patent is not considered as an obviousness art by Examiner.

Conclusion

Claims 5, 7-11, 15, 30 and 32 are rejected, and Claims 1-4, 6, 12-14, 28,29 and 31 are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is (703) 306-3483. The examiner can normally be reached from 9:00 a.m. to 5:00 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Christopher Low, can be reached on 703 308-2923. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.

SWL

Samuel W. Liu, Ph.D.

May 5, 2003

Karen Cochrane Carlson PhD

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER